

Application No. 09/933,680

Amendment Dated 10/22/2003

Reply to Notice of Allowance dated October 6, 2003

AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

✓ 1. (Currently amended) A method of treating an implantable biological tissue, said method comprising stabilizing glycosaminoglycans on the tissue and cross-linking proteins on the tissue, wherein the glycosaminoglycans stabilizing comprises contacting the tissue with (a) a water-soluble carbodiimide composition having a pH of 6.9 to 7.9, and wherein ~~the cross-linking comprises contacting the tissue with glutaraldehyde~~ (b) a carbohydrate oxidizing agent, or (c) a heterofunctional azide reagent.

✓ 2. (Original) The method of claim 1, wherein said glycosaminoglycans are endogenous to the tissue.

✓ 3. (Original) The method of claim 2, wherein the tissue is a part of an implantable bioprosthetic device.

✓ 4. (Original) The method of claim 3, wherein said device is selected from the group consisting of a heart valve prosthesis, a vascular graft, a skin graft, a dura mater graft, a cartilage graft, a cartilage implant, a pericardium graft, a urinary bladder prosthesis, a ligament prosthesis, and a tendon prosthesis.

✓ 5. (Original) The method of claim 4, wherein said device is a heart valve prosthesis.

✓ 6. (Original) The method of claim 5, wherein said heart valve prosthesis is selected from the group consisting of a porcine heart valve and a bovine pericardium-derived

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selected from the group consisting of a porcine heart valve and a bovine pericardium-derived heart valve prosthesis.

Claims 7-9 (Canceled)

✓10. (Previously presented) The method of claim 1, wherein the stabilization of glycosaminoglycans on the tissue is achieved prior to cross-linking proteins on the tissue.

✓11. (Original) The method of claim 10, wherein

a) the difference between i) the thermal shrinkage temperature of the tissue after contacting the tissue with said carbodiimide and ii) the thermal shrinkage temperature of the tissue prior to contacting the tissue with said carbodiimide is less than half of

b) the difference between i) the thermal shrinkage temperature of the tissue after cross-linking proteins on the tissue and ii) the thermal shrinkage temperature of the tissue prior to cross-linking proteins on the tissue.

✓12. (Previously presented) The method of claim 1, wherein said carbodiimide is 1-ethyl-3-(3-dimethyl aminopropyl) carbodiimide.

Claims 13-33 (Cancelled)

✓ 34. (Previously presented) A biological tissue treated by the method of claim 1.

35. (New) The method of claim 1, wherein the stabilizing of glycosaminoglycans on the tissue is achieved by contacting the tissue with the carbohydrate oxidizing agent to generate aldehyde groups on said glycosaminoglycans and the cross-linking is achieved by contacting the tissue with a bi-functional-carbohydrate-protein linking agent.

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✓36. (New) The method of claim 35, wherein said carbohydrate oxidizing agent is selected from the group consisting of bromine, periodate, nitric acid, and lead tetraacetate.

✓37. (New) The method of claim 35, wherein the bi-functional carbohydrate-protein linking agent is a member selected from the group consisting of glutaraldehyde, a diamine, and an azido hydrazide.

✓38. (New) The method of claim 1, wherein the stabilizing of glycosaminoglycans on the tissue is achieved by contacting the tissue with the heterofunctional azide reagent and the cross-linking is achieved by contacting the tissue with an agent for linking.

✓39. (New) The method of claim 38, wherein the agent for linking is a member selected from the group consisting of a dithiol, dithiothreitol, a di-aldehyde, glutaraldehyde, a di-carbonyl compound, a carbodiimide, and an epoxide.

✓40. (New) The method of claim 1, wherein the glycosaminoglycans are endogenous to the tissue.

✓41. (New) The method of claim 1, wherein the cross-linking comprises contacting the tissue with glutaraldehyde.

✓42. (New) The method of claim 1, wherein the cross-linking comprises contacting the tissue with glutaraldehyde, provided that the cross-linking is performed after the stabilizing of glycosaminoglycans.

43. (New) The method of claim 1, wherein the stabilizing comprises contacting the tissue with a water-soluble carbodiimide composition having a pH of 6.9 to 7.9, and the cross-linking comprises contacting the tissue with a cross-linking reagent, wherein the

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cross-linking reagent is a member selected from the group consisting of glutaraldehyde, formaldehyde, a dialdehyde, carbodiimide, and a polyepoxy ether.

44. (New) The method of claim 43, wherein the cross-linking reagent is glutaraldehyde.

✓ 45. (New) The method of claim 1, wherein the stabilizing comprises contacting the tissue with periodate and the cross-linking comprises contacting the tissue with glutaraldehyde.

46. (New) A method of treating an implantable biological tissue, said method comprising stabilizing glycosaminoglycans on the tissue and cross-linking proteins on the tissue, wherein the glycosaminoglycans stabilizing comprises contacting the tissue with a water-soluble carbodiimide composition having a pH of 6.9 to 7.9, and wherein the cross-linking comprises contacting the tissue with glutaraldehyde.

47. (New) A biological tissue treated by the method of claim 46.

✓ 48. (New) A method of treating an implantable biological tissue, said method comprising stabilizing glycosaminoglycans on the tissue and cross-linking proteins on the tissue, wherein the glycosaminoglycans stabilizing comprises contacting the tissue with periodate and wherein the cross-linking comprises contacting the tissue with glutaraldehyde.

✓ 49. (New) A biological tissue treated by the method of claim 48.